REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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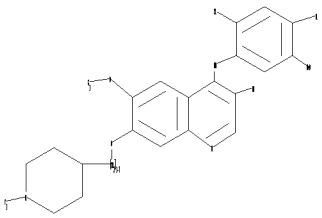

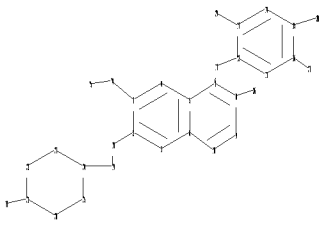

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17 18 19 26 27 28 29 33 34 35
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 20 21 22 23 24 25
chain bonds :
2-18 3-34 7-17 8-26 12-17 13-29 15-28 16-27 18-19 19-24 21-33 34-35
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-12 11-16 12-13 13-14
14-15 15-16 20-21 20-25 21-22 22-23 23-24 24-25
exact/norm bonds :
2-18 3-34 7-17 12-17 20-21 20-25 21-22 21-33 22-23 23-24 24-25 34-35

exact bonds :
8-26 13-29 15-28 16-27 18-19 19-24
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-12 11-16 12-13 13-14
14-15 15-16

G1:CH3,Et,n-Pr,i-Pr

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
20:Atom 21:Atom
22:Atom 23:Atom 24:Atom 25:Atom 26:CLASS 27:CLASS 28:CLASS 29:CLASS
33:CLASS 34:CLASS
35:CLASS

L1 STRUCTURE UPLOADED

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SAMPLE SCREEN SEARCH COMPLETED -        1 TO ITERATE

100.0% PROCESSED        1 ITERATIONS                                 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            1 TO       80
PROJECTED ANSWERS:               1 TO       80

L2            1 SEA SSS SAM L1

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FULL SEARCH INITIATED 16:07:05 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -        9 TO ITERATE

100.0% PROCESSED        9 ITERATIONS                                 7 ANSWERS
SEARCH TIME: 00.00.01

L3            7 SEA SSS FUL L1

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L3   ANSWER 1 OF 7  REGISTRY  COPYRIGHT 2008 ACS on STN
RN   753005-95-7  REGISTRY
ED   Entered STN:  28 Sep 2004
CN   3-Quinolinecarbonitrile, 4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-ethoxy-
     7-[2-(1-methyl-4-piperidinyl)ethoxy]-  (CA INDEX NAME)
OTHER NAMES:
CN   4-[(2,4-Dichloro-5-methoxyphenyl)amino]-6-ethoxy-7-[2-(1-methylpiperidin-4-
     yl)ethoxy]quinoline-3-carbonitrile
MF   C27 H30 Cl2 N4 O3
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPATFULL
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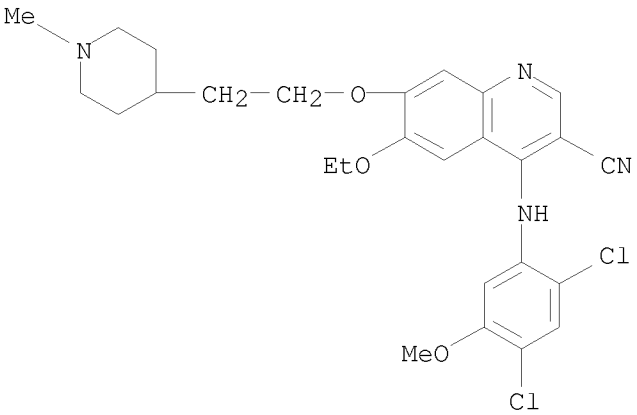


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

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               4 REFERENCES IN FILE CAPLUS (1907 TO DATE)
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L3 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2008 ACS on STN
RN 753005-93-5 REGISTRY
ED Entered STN: 28 Sep 2004
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OTHER NAMES:
CN 4-[(2,4-Dichloro-5-methoxyphenyl)amino]-6-ethoxy-7-[3-(1-methylpiperidin-4-
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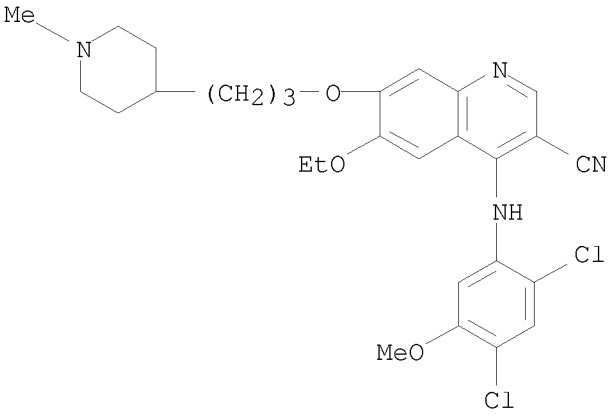
MF C28 H32 Cl2 N4 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2008 ACS on STN
RN 753005-91-3 REGISTRY
ED Entered STN: 28 Sep 2004
CN 3-Quinolinecarbonitrile, 4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-ethoxy-
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OTHER NAMES:
CN 4-[(2,4-Dichloro-5-methoxyphenyl)amino]-6-ethoxy-7-[(1-methylpiperidin-4-
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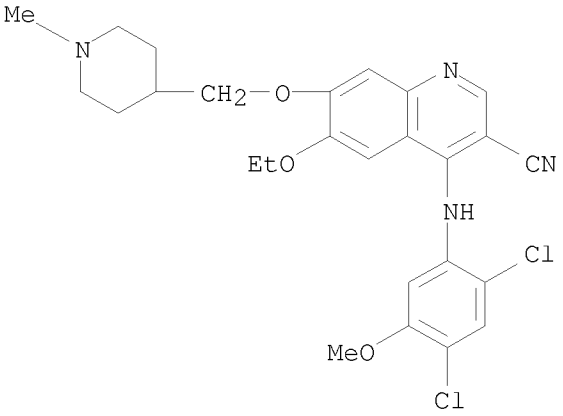
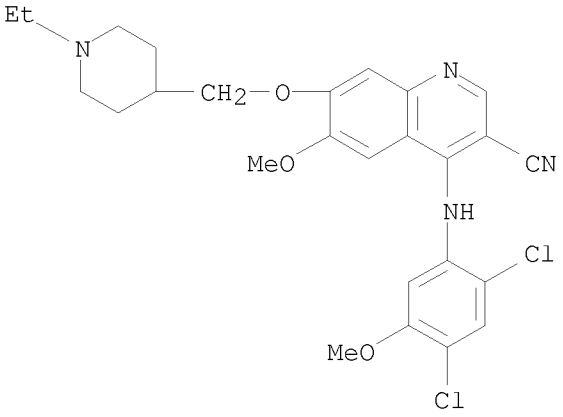
MF C26 H28 Cl2 N4 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2008 ACS on STN
RN 622369-25-9 REGISTRY
ED Entered STN: 01 Dec 2003
CN 3-Quinolinecarbonitrile, 4-[(2,4-dichloro-5-methoxyphenyl)amino]-7-[(1-ethyl-4-piperidinyl)methoxy]-6-methoxy- (CA INDEX NAME)
OTHER NAMES:
CN 4-[(2,4-Dichloro-5-methoxyphenyl)amino]-7-[(1-ethyl-piperidin-4-yl)methoxy]-6-methoxyquinoline-3-carbonitrile
MF C26 H28 Cl2 N4 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL



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6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2008 ACS on STN
RN 622369-21-5 REGISTRY
ED Entered STN: 01 Dec 2003
CN 3-Quinolinecarbonitrile, 4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-methoxy-
    7-[3-(1-methyl-4-piperidinyl)propoxy]- (CA INDEX NAME)
OTHER NAMES:
CN 4-[(2,4-Dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[3-(1-methyl-piperidin-
    4-yl)propoxy]quinoline-3-carbonitrile
MF C27 H30 Cl2 N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, PROUSDDR, SYNTHLINE, TOXCENTER, USPAT2,
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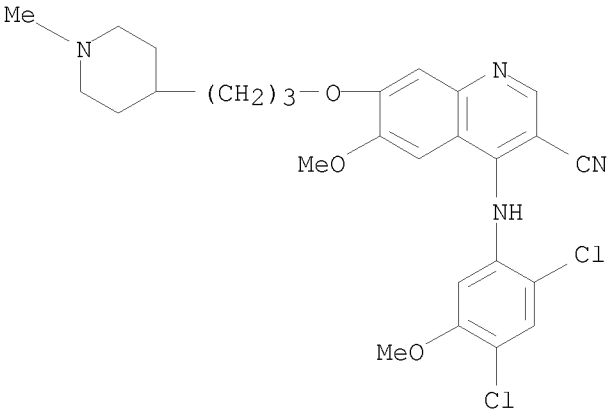
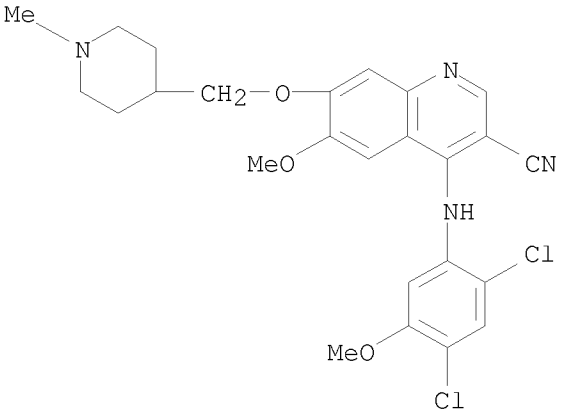


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

              8 REFERENCES IN FILE CA (1907 TO DATE)
              8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

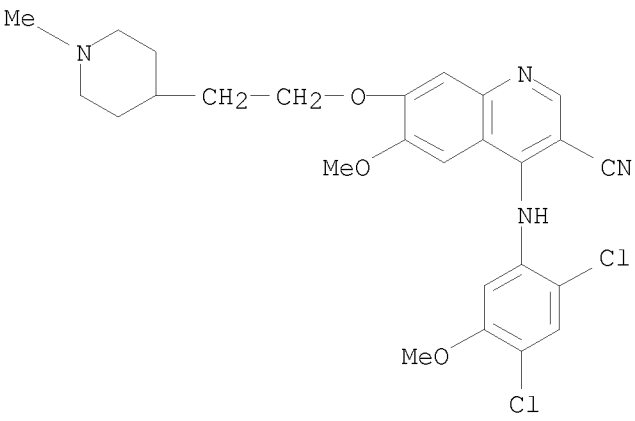
L3 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2008 ACS on STN
RN 622368-91-6 REGISTRY
ED Entered STN: 01 Dec 2003
CN 3-Quinolinecarbonitrile, 4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-methoxy-
    7-[(1-methyl-4-piperidinyl)methoxy]- (CA INDEX NAME)
OTHER NAMES:
CN 4-[(2,4-Dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[(1-methyl-4-
    piperidinyl)methoxy]-3-quinolinecarbonitrile
MF C25 H26 Cl2 N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, PROUSDDR, SYNTHLINE, TOXCENTER, USPAT2,
      USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1907 TO DATE)
9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2008 ACS on STN
RN 622368-88-1 REGISTRY
ED Entered STN: 01 Dec 2003
CN 3-Quinolinecarbonitrile, 4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[2-(1-methyl-4-piperidinyl)ethoxy]- (CA INDEX NAME)
OTHER NAMES:
CN 4-[(2,4-Dichloro-5-methoxyphenyl)amino] 6-methoxy-7-[2-(1-methylpiperidin-4-yl)ethoxy]-3-quinolinecarbonitrile
MF C26 H28 Cl2 N4 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8 REFERENCES IN FILE CA (1907 TO DATE)
8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                 194.20     194.62

FILE 'CAPLUS' ENTERED AT 16:08:49 ON 10 JAN 2008
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=> s l3
L4           9 L3

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5            9 DUP REM L4 (0 DUPLICATES REMOVED)

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L5   ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2007:17766  CAPLUS <<LOGINID::20080110>>
DOCUMENT NUMBER:          146:75345
TITLE:                    Inhibition of osteolytic lesions by
                          quinolinecarbonitrile derivative src kinase inhibitors
INVENTOR(S):              Darnay, Bryant G.; Price, Janet E.; Poblenz, Ann;
                          Talpaz, Moshe
PATENT ASSIGNEE(S):       The Board of Regents of the University of Texas
                          System, USA
SOURCE:                   U.S. Pat. Appl. Publ., 23pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     US 2007004748         A1    20070104    US 2006-455272          20060616
PRIORITY APPLN. INFO.:                       US 2005-691933P     P   20050617
OTHER SOURCE(S):          MARPAT 146:75345
AB   The invention discloses methods and compns. for treating bone-resorbing
     diseases or bone resorption related to a pathol. condition generally,
     including, but not limited to osteoporosis, arthritis, rheumatoid
     arthritis, cancer metastases to the bone, bone cancer, hypercalcemia,
     osteolytic lesions with orthopedic implants, Paget's disease, and bone
     loss associated with hyperparathyroidism.  Representative cancers include,
     but are not limited to, breast cancer, prostrate cancer, colon cancer,
     endometrial cancer, multiple myeloma, renal cell carcinoma, heck and neck
     cancers, and cervical carcinoma.  Arthritic conditions include, but are
     not limited to, adjuvant-, collagen-, bacterial- and antigen-induced
     arthritis, particularly rheumatoid arthritis.
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L5 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1356765 CAPLUS <<LOGINID::20080110>>
DOCUMENT NUMBER: 146:75337
TITLE: Inhibition of osteolytic lesions by SRC kinase inhibitors
INVENTOR(S): Darnay, Bryant G.; Price, Janet E.; Poblenz, Ann; Talpaz, Moshe
PATENT ASSIGNEE(S): Board of Regents, The University of Texas System, USA
SOURCE: PCT Int. Appl., 47pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006138590	A1	20061228	WO 2006-US23529	20060616

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-691933P P 20060617
OTHER SOURCE(S): MARPAT 146:75337
AB The present invention include methods and compns. for treating bone-resorbing diseases or bone resorption related to a pathol. condition generally, including, but not limited to osteoporosis, arthritis, rheumatoid arthritis, cancer metastases to the bone, bone cancer, hypercalcemia, osteolytic lesions with orthopedic implants, Paget's disease, and bone loss associated with hyperparathyroidism. Representative cancers include, but are not limited to breast cancer, prostrate cancer, colon cancer, endometrial cancer, multiple myeloma, renal cell carcinoma, head and neck cancers, and cervical carcinoma. Arthritic conditions include, but are not limited to adjuvant-, collagen-, bacterial- and antigen-induced arthritis, particularly rheumatoid arthritis.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:409267 CAPLUS <<LOGINID::20080110>>
DOCUMENT NUMBER: 142:481956
TITLE: 4-Anilino-3-quinolinecarbonitriles for the treatment of chronic myelogenous leukemia (CML)
INVENTOR(S): Boschelli, Frank; Arndt, Kim T.; Golas, Jennifer M.
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: U.S. Pat. Appl. Publ., 12 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2005101780	A1	20050512	US 2004-980097		20041103
AU 2003291245	A1	20040606	AU 2003-291245		20031106
WO 2005047259	A1	20050526	WO 2003-US35322		20031106
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AU 2004289243	A1	20050526	AU 2004-289243		20041103
CA 2543163	A1	20050526	CA 2004-2543163		20041103
WO 2005046693	A1	20050526	WO 2004-US36722		20041103
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EP 1680119	A1	20060719	EP 2004-800721		20041103
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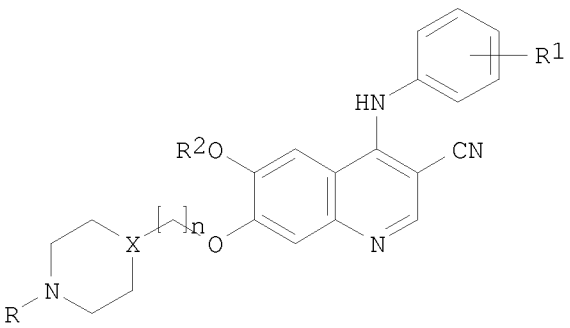
CN 1874776	A	20061206	CN 2004-80032311		20041103
BR 2004016289	A	20070123	BR 2004-16289		20041103
JP 2007533655	T	20071122	JP 2006-539641		20041103
MX 2006PA04744	A	20060705	MX 2006-PA4744		20060427
IN 2006KN01122	A	20070427	IN 2006-KN1122		20060502
NO 2006002255	A	20060801	NO 2006-2255		20060519
PRIORITY APPLN. INFO.:			US 2003-517819P	P	20031106
			WO 2003-US35322	A	20031106
			WO 2004-US36722	W	20041103

OTHER SOURCE(S): MARPAT 142:481956

GI



I

AB The invention provides compds. I [n = 1-3; X = N, CH, provided that when X

= N, n = 2 or 3; R = alkyl; R1 = 2,4-Cl2-5-OMe; 2,4-Cl2; 3,4,5-(MeO)3; 2-Cl-5-(MeO); 2-Me-5-OMe; 2,4-(Me)2; 2,4-(Me)2-5-OMe; 2,4-CL2-5-OEt; R2 = alkyl], useful as Src and Abl kinase inhibitors. Over twenty compds. I were prepared (no details of preparation given) and tested against Src kinase. Thus, 4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[3-(4-methyl-1-piperazinyl)propoxy]-3-quinolinecarbonitrile showed IC50 of 1.2 nM against Src enzyme. The pharmaceutical composition comprising the compound I is disclosed.

L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:544555 CAPLUS <<LOGINID::20080110>>
DOCUMENT NUMBER: 143:208056
TITLE: 3D-QSAR studies on c-Src kinase inhibitors and docking analyses of a potent dual kinase inhibitor of c-Src and c-Abl kinases
AUTHOR(S): Thaimattam, Ram; Daga, Pankaj R.; Banerjee, Rahul; Iqbal, Javed
CORPORATE SOURCE: Department of Molecular Modeling and Drug Design, Dr. Reddy's Laboratories Ltd, Hyderabad, Miyapur, 500 049, India
SOURCE: Bioorganic & Medicinal Chemistry (2005), 13(15), 4704-4712
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Three-dimensional quant. structure-activity relationship (3D-QSAR) analyses were carried out on quinazoline, quinoline, and cyanoquinoline derivs. inhibiting c-Src kinase. Comparative mol. field anal. (CoMFA) and comparative mol. similarity indexes anal. (CoMSIA) 3D-QSAR models were developed. The conventional r2 values for CoMFA and CoMSIA are 0.93 and 0.89, resp. In addition, a homol. model of c-Src kinase with the activation loop resembling the active conformation was constructed using the crystal structure of the kinase domain of Lck. The ATP binding pocket of the active form of c-Src is similar to that of the c-Abl kinase in which the activation loop resembles that of an active form. One of the potent c-Src and c-Abl dual kinase inhibitors (77 or SKI-606) was docked inside the active sites of both c-Src and c-Abl. The orientation and hydrogen bonding interactions of 77 are similar in both kinases. The results of 3D-QSAR analyses and structure based studies will be useful for the design of novel c-Src and c-Abl dual kinase inhibitors.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:740166 CAPLUS <<LOGINID::20080110>>
DOCUMENT NUMBER: 141:243354
TITLE: Preparation of 4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-alkoxy-3-quinolinecarbonitriles as Src inhibitors for the treatment of ischemic injury
INVENTOR(S): Boschelli, Diane Harris; Zaleska, Margaret Maria; Boschelli, Frank Charles; Arndt, Kim Timothy
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2004075898	A1	20040910	WO 2004-US4904	20040219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
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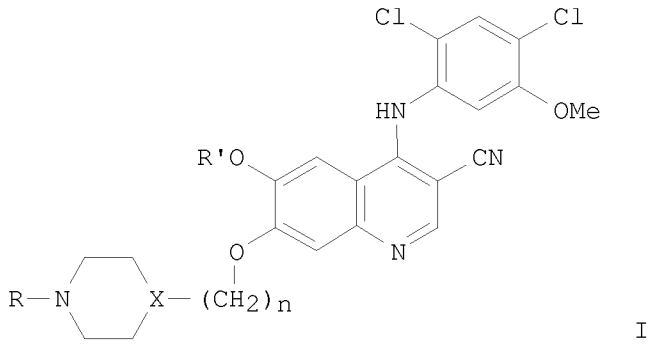
US 2004229880	A1	20041118	US 2004-780973	20040218
AU 2004216235	A1	20040910	AU 2004-216235	20040219
CA 2516418	A1	20040910	CA 2004-2516418	20040219
EP 1594502	A1	20051116	EP 2004-712889	20040219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004007441	A	20060131	BR 2004-7441	20040219
CN 1750824	A	20060322	CN 2004-80004674	20040219
JP 2006522023	T	20060928	JP 2006-503706	20040219
IN 2005KN01564	A	20070126	IN 2005-KN1564	20050808
MX 2005PA08706	A	20051005	MX 2005-PA8706	20050816
NO 2005004070	A	20051114	NO 2005-4070	20050901
PRIORITY APPLN. INFO.:			US 2003-449316P P	20030221
			WO 2004-US4904 A	20040219

OTHER SOURCE(S): MARPAT 141:243354

GI



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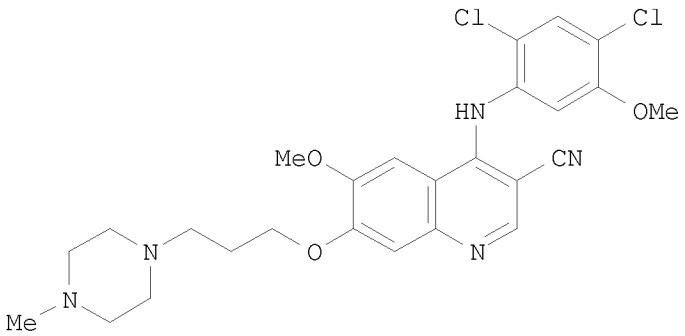

II

AB Title compds. I [wherein X = N, CH; n = 1-3; R', R = independently C1-3 alkyl; with the proviso that when n = 1, X ≠ N; and pharmaceutically

acceptable salts thereof] were prepared as Src inhibitors. Compds. of the invention and their pharmaceutical compns. provide neuroprotection, inhibit neurol. deficits, reduce infarct vols., and inhibit post-ischemic vascular permeability following an ischemic event. For example, amination of 7-(3-chloropropoxy)-4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-methoxy-3-quinolinecarbonitrile with N-methylpiperazine provided II (75%). The latter suppressed Src tyrosine kinase activity (IC50 = 1.2 nM) and inhibited Src dependent cell proliferation in Rat2 fibroblasts stably transformed with a plasmid containing the catalytic domain of human c-Src (IC50 = 100 nM). In a transient model of focal ischemia using Wistar rats, administration of II at doses of 3, 10, and 30 mg/kg (IV) resulted in reduction of brain tissue infarction volume by 22%, 53%, and 42%, resp., and reduction of stroke-induced neurol. deficits as measured by mean motor deficit scores. In a model producing extensive infarction to sensorimotor cortex with quant. assessment of neurol. deficits for 21 days post-stroke, II provided significant improvement in the neurol. outcome.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:158504 CAPLUS <<LOGINID::20080110>>

DOCUMENT NUMBER: 140:357180

TITLE: 7-Alkoxy-4-phenylamino-3-quinolinecarbonitriles as Dual Inhibitors of Src and Abl Kinases

AUTHOR(S): Boschelli, Diane H.; Wang, Yanong D.; Johnson, Steve; Wu, Biqi; Ye, Fei; Sosa, Ana Carolina Barrios; Golas, Jennifer M.; Boschelli, Frank

CORPORATE SOURCE: Chemical and Screening Sciences and Oncology, Wyeth Research, Pearl River, NY, 10965, USA

SOURCE: Journal of Medicinal Chemistry (2004), 47(7), 1599-1601
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:357180

AB 7-Alkoxy-4-phenylamino-3-quinolinecarbonitriles were prepared by several routes and are potent inhibitors of Src and Abl kinase activity.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:892755 CAPLUS <<LOGINID::20080110>>

DOCUMENT NUMBER: 139:364842

TITLE: Process for the preparation of 7-substituted 3-quinoline and 3-quinol-4-one carbonitriles via nucleophilic substitution

INVENTOR(S): Boschelli, Diane Harris; Wang, Yanong Daniel; Johnson, Steven Lawrence; Berger, Dan Maarten

PATENT ASSIGNEE(S): Wyeth Holdings Corporation, USA

SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003093241	A1	20031113	WO 2003-US13149	20030429
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

TW 275390	B	20070311	TW 2003-92109893		20030428
CA 2483529	A1	20031113	CA 2003-2483529		20030429
AU 2003231162	A1	20031117	AU 2003-231162		20030429
EP 1499594	A1	20050126	EP 2003-724293		20030429
EP 1499594	B1	20050817			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

BR 2003009712	A	20050215	BR 2003-9712		20030429
CN 1665787	A	20050907	CN 2003-815201		20030429
AT 302191	T	20050915	AT 2003-724293		20030429
JP 2005529907	T	20051006	JP 2004-501380		20030429
ES 2243903	T3	20051201	ES 2003-3724293		20030429
NZ 536141	A	20060331	NZ 2003-536141		20030429
RU 2309149	C2	20071027	RU 2004-134735		20030429
IN 2004KN01490	A	20060616	IN 2004-KN1490		20041006
NO 2004004533	A	20041129	NO 2004-4533		20041021
MX 2004PA10664	A	20050125	MX 2004-PA10664		20041027
ZA 2004009639	A	20060628	ZA 2004-9639		20041129
HK 1070358	A1	20051104	HK 2005-103003		20050408
PRIORITY APPLN. INFO.:			US 2002-376456P	P	20020430
			WO 2003-US13149	W	20030429

OTHER SOURCE(S): CASREACT 139:364842; MARPAT 139:364842
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A new process for preparing quinoline I, quinolone II, their intermediates and pharmaceutical salts, which are highly effective as inhibitors of protein kinases useful in the treatment of cancer, via nucleophilic substitution is provided [wherein X = O, S, NH, NR2'; W = H, OR3; R1 = (un)substituted alkyl, cycloalkyl, (un)substituted (fused) hetero/aryl; R2, R2', R3 = (un)substituted alk(en/yn)yl, or (un)substituted aryl, hetero(aryl/cyclyl) optionally attached to a linear chain which may contain O, S(O)m, or N-alkyl, or R2R2'N = (un)substituted heterocycle; m = 0-2]. Specifically, 7-fluoro-4-oxo-1,4-dihydro-3-quinolinecarbonitriles were converted in three steps to 7-substituted-3-quinolinecarbonitriles by halogenation with POCl3 or POBr3, substitution of 4-halo-3-quinolinecarbonitrile intermediate with an amine R1NH2 in the presence of Py•HCl, and substitution of 7-fluoro-3-quinolinecarbonitrile with a compound of formula R2XH [wherein R1, R2, and X are defined as above]. III was prepared by reacting IV (preparation given) with POCl3 at reflux, N-alkylation of 2,4-dichloro-5-methoxy-aniline with the resulting 4-chloroquinoline-3-carbonitrile intermediate in 2-ethoxyethanol at 120° in the presence of Py•HCl, followed by addition of 7-fluoroquinoline-3-carbonitrile to a preheated mixture of 2-butyn-1-ol and Na and reaction overnight at 120°.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:892085 CAPLUS <<LOGINID::20080110>>
DOCUMENT NUMBER: 139:381383
TITLE: Process for the preparation of 7-substituted 3-quinoline and 3-quinol-4-one carbonitriles via nucleophilic substitution
INVENTOR(S): Boschelli, Diane Harris; Wang, Yanong Daniel; Johnson, Steve Lawrence; Berger, Dan Maarten
PATENT ASSIGNEE(S): Wyeth Holdings Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 30 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003212276	A1	20031113	US 2003-425765		20030429
US 6780996	B2	20040824			
TW 275390	B	20070311	TW 2003-92109893		20030428
CN 1665787	A	20050907	CN 2003-815201		20030429
ES 2243903	T3	20051201	ES 2003-3724293		20030429
ZA 2004009639	A	20060628	ZA 2004-9639		20041129
PRIORITY APPLN. INFO.:			US 2002-376456P	P	20020430

OTHER SOURCE(S): MARPAT 139:381383
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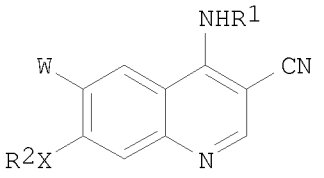

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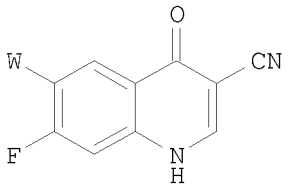

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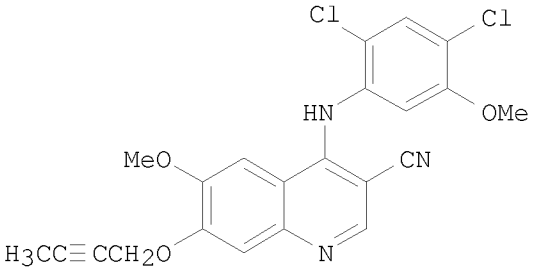

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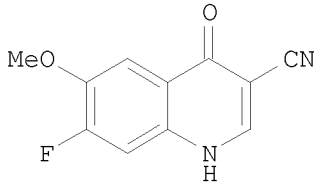

IV

AB A new process for preparing quinoline I, quinolone II, their intermediates and pharmaceutical salts, which are highly effective as inhibitors of protein kinases useful in the treatment of cancer, via nucleophilic substitution is provided [wherein X = O, S, NH, NR2'; W = H, OR3; R1 = (un)substituted alkyl, cycloalkyl, (un)substituted (fused) hetero/aryl; R2, R2', R3 = (un)substituted alk(en/yn)yl, or (un)substituted aryl, hetero(aryl/cyclyl) optionally attached to a linear chain which may

contain O, S(O)m, or N-alkyl, or R2R2'N = (un)substituted heterocycle; m = 0-2]. Specifically, 7-fluoro-4-oxo-1,4-dihydro-3-quinolinecarbonitriles were converted in three steps to 7-substituted-3-quinolinecarbonitriles by halogenation with POCl3 or POBr3, substitution of 4-halo-3-quinolinecarbonitrile intermediate with an amine R1NH2 in the presence of Py•HCl, and substitution of 7-fluoro-3-quinolinecarbonitrile with a compound of formula R2XH [wherein R1, R2, and X are defined as above]. III was prepared by reacting IV (preparation given) with POCl3 at reflux, N-alkylation of 2,4-dichloro-5-methoxy-aniline with the resulting 4-chloroquinoline-3-carbonitrile intermediate in 2-ethoxyethanol at 120° in the presence of Py•HCl, followed by addition of 7-fluoroquinoline-3-carbonitrile to a preheated mixture of 2-butyn-1-ol and Na and reaction overnight at 120°.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:795104 CAPLUS <<LOGINID::20080110>>

DOCUMENT NUMBER: 140:42015

TITLE: Investigation of the effect of varying the 4-anilino and 7-alkoxy groups of 3-quinolinecarbonitriles on the inhibition of Src kinase activity

AUTHOR(S): Boschelli, Diane H.; Ye, Fei; Wu, Biqi; Wang, Yanong D.; Barrios Sosa, Ana Carolina; Yaczko, Deanna; Powell, Dennis; Golas, Jennifer M.; Lucas, Judy; Boschelli, Frank

CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Pearl River, NY, 10965, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(21), 3797-3800
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:42015

AB Several 7-alkoxy-4-anilino-3-quinolinecarbonitriles were synthesized and evaluated for Src kinase inhibitory activity. Optimal inhibition of both Src enzymic and cellular activity was seen with analogs having a 2,4-dichloro-5-methoxyaniline group at C-4. 4-[(2,4-Dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[(1-methyl-4-piperidinyl)methoxy]-3-quinolinecarbonitrile which has a 1-methylpiperidinemethoxy group at C-7, showed in vivo activity in a xenograft model. Compds. thus prepared and tested included 4-(2,4-dichlorophenyl)-6,7-bis(2-methoxyethoxy)-3-quinolinecarbonitrile, 4-(2,4-dichloro-5-methoxyphenyl)-6,7-bis(2-methoxyethoxy)-3-quinolinecarbonitrile, 6,7-bis(2-methoxyethoxy)-4-(3,4,5-trimethoxyphenyl)-3-quinolinecarbonitrile, 4-[(2,4-dichlorophenyl)amino]-6-methoxy-7-(2-methoxyethoxy)-3-quinolinecarbonitrile.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FULL ESTIMATED COST	45.17	239.79

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-7.20	-7.20

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DICTIONARY FILE UPDATES: 9 JAN 2008 HIGHEST RN 960280-26-6

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